

CLAIMS

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1. An isolated Fv protein, comprising:

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a) a variable region of a heavy chain of a monoclonal antibody that binds the antigen specifically bound by monoclonal antibody 8H9 and a variable region of a light chain of the monoclonal antibody that binds the antigen specifically bound by monoclonal antibody 8H9; and

b) an effector molecule comprising a toxin;

wherein the Fv protein specifically binds the epitope bound by monoclonal antibody 8H9.

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2. The isolated Fv protein of claim 1, wherein said effector molecule comprises ricin A, abrin, diphtheria toxin or a subunit thereof, *Pseudomonas* exotoxin or a portion thereof, saporin, restrictocin or gelonin.

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3. The isolated Fv protein of claim 2, wherein said effector molecule is selected from the group consisting of PE38, PE40, PE38KDEL, and PE38REDL.

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4. The isolated Fv protein of claim 1, wherein the variable region of the heavy chain comprises an amino acid sequence set forth as SEQ ID NO: 7, and wherein the variable region of the light chain comprises an amino acid sequence set forth as SEQ ID NO: 8.

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5. The isolated Fv protein of claim 1, wherein the isolated Fv protein is an isolated single chain fusion protein comprising the variable region of a heavy chain of a monoclonal antibody that binds the antigen specifically bound by monoclonal antibody 8H9 and the variable region of a light chain of the monoclonal antibody that binds the antigen specifically bound by monoclonal antibody 8H9.

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6. The isolated Fv protein of claim 1, wherein the variable region of the heavy chain comprises
- a heavy chain framework region comprising a complementarity determining region HCDR1, a HCDR2, and a HCDR3, wherein the (HCDR)-1 comprises an amino sequence NYDIN (amino acids 31-35 of SEQ ID NO: 3) the HCDR2 comprising an amino acid sequence WIFPGDGSTQY (amino acids 50-60 of SEQ ID NO: 3), the HCDR3 comprises an amino acid sequence QTTATWFAY (amino acids 99-107 of SEQ ID NO: 3).
7. The isolated Fv protein of claim 1, wherein the variable region of the light chain comprises
- a light chain framework region comprising a complementarity determining region (LCDR)1, a LCDR2, and a LCDR3, wherein the LCDR1 comprises an amino acid sequence RASQSISDYLH (amino acids 157-167 of SEQ ID NO: 3), the LCDR2 comprises an amino acid sequence YASQSSIS (amino acids 183-189 of SEQ ID NO: 3), and the LCDR3 comprises an amino acid sequence QNGHSFPLT (amino acids 222-230 of SEQ ID NO: 3).
8. The isolated Fv protein of claim 6, wherein the heavy chain framework and the light chain framework are human.
9. The isolated Fv protein of claim 1, wherein the variable region of a heavy chain of a monoclonal antibody that binds the antigen specifically bound by monoclonal antibody 8H9 and the variable region of a light chain of the monoclonal antibody that binds the antigen specifically bound by monoclonal antibody 8H9 are covalently linked by disulfide bonds.
10. The isolated Fv protein of claim 9, wherein the toxin is covalently linked to the variable region of the heavy chain.
11. The isolated Fv protein of claim 10, wherein the toxin comprises a *Pseudomonas* exotoxin.

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12. The isolated Fv protein of claim 11, wherein the *Pseudomonas* exotoxin is PE38.

5 13. The Fv of claim 1, wherein said Fv polypeptide comprises an amino acid sequence set forth as SEQ ID NO: 7 and an amino acid sequence set forth as SEQ ID NO: 8.

10 14. A recombinant nucleic acid molecule encoding
a) a *Pseudomonas* exotoxin; and
b) a heavy chain of a monoclonal antibody that specifically binds the antigen bound by monoclonal antibody 8H9;

wherein transcription and translation of the nucleic acid produces a fusion protein comprising the *Pseudomonas* exotoxin and the heavy chain of the antibody.

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15. The recombinant nucleic acid molecule of claim 14, wherein the nucleic acid encodes an amino acid sequence set forth as SEQ ID NO:7

20 16. The recombinant nucleic acid molecule of claim 14, wherein the *Pseudomonas* exotoxin is selected from the group consisting of PE38, PE40, PE38KDEL and PE38REDL.

25 17. The recombinant nucleic acid molecule of claim 14, wherein the Fv region comprises a human heavy chain framework.

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18. A recombinant DNA molecule that encodes a single chain antibody and an immunotoxin, said recombinant DNA molecule comprising
a DNA sequence that encodes the Fv region of both the light and heavy chains of an antibody fused to form a single molecule that has the binding specificity
30 of monoclonal antibody 8H9 and an effector molecule.

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19. The recombinant DNA molecule of claim 18, wherein said antibody comprises the heavy chain complementarity determining regions (HCDR)-1, HCDR-2, and HCDR-3 of monoclonal antibody 8H9, and the light chain complementarity determining regions LCDR-1, LCDR-2, and LCDR-3 of monoclonal antibody 8H9.

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20. The recombinant nucleic acid molecule of claim 18, wherein the effector molecule comprises PE38, PE40, PE38KDEL or PE38REDL

21. A pharmaceutical composition comprising a therapeutically effective amount of the isolated Fv protein of claim 1 sufficient to inhibit tumor cell growth, and a pharmaceutically acceptable carrier.

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22. The composition of claim 21, wherein said effector molecule is a *Pseudomonas* exotoxin.

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23. The composition of claim 21, wherein the *Pseudomonas* exotoxin molecule comprises PE38, PE40, PE38KDEL or PE38REDL.

24. A method for killing a tumor cell, comprising contacting the cell with an effective amount of the isolated Fv protein of claim 1, thereby killing the cell.

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25. The method of claim 24, wherein the cell is in vitro.

26. The method of claim 24, wherein the cell is in vivo.

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27. The method of claim 24, wherein the Fv protein comprises an effector molecule comprising ricin A, abrin, diphtheria toxin or a subunit thereof, *Pseudomonas* exotoxin or a portion thereof, saporin, restrictocin or gelonin.

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28. The method of claim 27, wherein the effector molecule comprises a *Pseudomonas* exotoxin.

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29. The method of claim 28, wherein the *Pseudomonas* exotoxin comprises PE35, PE37, PE38 or PE40.

30. The method of claim 29, wherein the *Pseudomonas* exotoxin is PE38.

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31. The method of claim 24, wherein the cell is a breast cancer cell, an osteosarcoma cell, or a neuroblastoma cell.

32. A method for treating a tumor in a subject, comprising administering to the subject a therapeutically effective amount of the Fv protein of claim 1, thereby treating the tumor.

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33. The method of claim 32, wherein the tumor is a breast cancer, an osteosarcoma, or a neuroblastoma.

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34. The method of claim 32, wherein the single chain fusion protein comprises effector molecule comprises ricin A, abrin, diphtheria toxin or a subunit thereof, *Pseudomonas* exotoxin or a portion thereof, saporin, restrictocin or gelonin.

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35. The method of claim 34, wherein the single chain fusion protein comprises a *Pseudomonas* exotoxin.

36. The method of claim 35, wherein the *Pseudomonas* exotoxin comprises PE35, PE37, PE38 or PE40.

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37. The method of claim 36, wherein the *Pseudomonas* exotoxin is PE38.

38. Use of an isolated Fv protein, comprising (a) a Fv polypeptide comprising both the light and the heavy chains of an antibody that binds the antigen specifically bound by 8H9; and (b) an effector molecule comprising a toxin covalently linked to the Fv polypeptide, for the manufacture of a medicament for the treatment of a tumor.

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